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10/638,173	08/06/2003	Robert Kain	ILLINC.026C1	3813

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EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/638,173	KAIN ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *60,65-71,76-83,88-96,101-117 and 126-157* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60,65-71,76-83,88-96,101-117 and 126-157* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8 April 2010 has been entered.

Status of the Claims

2. This action is in response to papers filed 8 April 2010 in which claim 60 was amended and claims 142-157 were added. All of the amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 9 October 2009 under 35 U.S.C. 103(a) are maintained. Applicant's arguments have been thoroughly reviewed and are discussed below. New grounds for rejection, necessitated by the amendments, are discussed.

Claims 60, 65-71, 76-83, 88-96, 101-117 and 126-157 are under prosecution.

Priority

3. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. The Provisional Application filed 10 February 2000 upon which priority is claimed does not provide adequate support under 35 U.S.C. 112 for Claims 60, 65-71, 76-83, 88-96,

101-117 and 126-157 of the instant application. The instant claims are drawn to an array having a second population of microspheres randomly distributed to assay locations on the array wherein the second population comprises blank microspheres. The '631 provisional application does not support the instantly claimed second population. Therefore the effective filing date for the instant claims is the filing date of parent application 09/782,588 i.e. 12 February 2001.

Information Disclosure Statement

4. The IDS submitted 27 August 2009 was considered on 9 October 2009. However a copy of the initialed 1449 was not attached to the Office Action of 9 October 2009. A copy of the initialed 1449 is attached to this action.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 60, 66-71, 77-83, 89-96, 103-104, 106-117, 127, 129 and 131-141 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (U.S. Patent No.

6,327,410, filed 11 September 1998) as evidence by Chee (U.S. Patent No. 6,544,732, filed 20 May 1999) in view of McDevitt et al (U.S. Patent No. 6,680,206, filed 16 July 1999) and/or Seul et al (U.S. Patent No. 7,041,510, filed 17 September 1999).

Regarding Claim 60, 71, 83, 94, Walt et al disclose an array and method of making the array comprising a substrate having a surface (Column 5, lines 32-60), a first assay location and second assay location on the surface (Column 5, line 61-Column 6, line 30), wherein the substrate has a first plurality of depressions in first and second assay locations and first and second microsphere populations randomly placed in the assay locations wherein the assay locations spatially identifiable (Column 18, line 59-Column 18, line 5).

Walt teaches the array and method wherein the bioactive agents are attached to "blank microspheres" to provide the subpopulations (Column 12, lines 3-8). Chee (Column 8, lines 23-27) teaches:

> Each microsphere comprises a bioactive agent, although as will be appreciated by those in the art, there may be some microspheres which do not contain a bioactive agent, depending the on the synthetic methods.(emphasis added)

Hence, one of skill in the art would appreciate that each population of Walt would likely include a subpopulation of blank microspheres.

Furthermore, blank beads were well known and routinely practiced in the art of bead arrays at the time the invention was made as taught by McDevitt and Seul.

McDevitt et al teach a similar array and method of making the array comprising a substrate having a surface (Fig. 3), a first assay location and second assay location on

the surface (#250, Fig. 3, Column 39, lines 15-34 and Column 40, lines 34-37), a first plurality of depressions in first and second assay locations and first and second microsphere populations randomly placed in the assay locations (Column 10, lines 13-16) and wherein assay locations comprises blank microspheres (Column 25, lines 1-45 and Fig. 16) wherein the blank microspheres provide a reference signal to which multiple different signals can be compared thereby allowing simultaneous evaluation of multiple chemically distinct analytes (Column 25, lines 1-8).

Seul also teach a similar array and method of making the array comprising a substrate having multiple assay locations and multiple populations of beads randomly distributed in the assay locations (e.g. Fig. 28) wherein the assay locations further comprise blank beads (i.e. spacer particles) to provide interparticle spacing of analyte beads and thereby allowing optical analysis of individual analyte particles (Column 25, lines 2-21).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the blank beads of McDevitt and/or Seul to the array of Walt. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success and for the added benefits of providing appropriate spacing of analyte beads allowing optical analysis of individual analyte particles (Seul, Column 25, lines 2-21) and/or providing a reference signal to which multiple different signals can be compared allowing simultaneous evaluation of multiple chemically distinct analytes (McDevitt, Column 25, lines 1-8).

Regarding Claim 66, 77, 89, Walt et al teach the array wherein the bioactive agent comprises a nucleic acid (Column 10, lines 28-35). McDevitt et al disclose the array wherein the bioactive agent comprises a nucleic acid (Column 5, lines 45-65) and Seul et al teach the bioactive agent comprises a nucleic acid (Example IX).

Regarding Claims 68, 79, 91, 103, Walt et al teach the array is within a hybridization chamber (Fig. 4). McDevitt et al teach the similar array wherein the substrate is enclosed within a hybridization chamber (Fig. 17, Column 26-27).

Regarding Claims 69, 80, 92, 104, Walt et al teach the array wherein the substrate comprises a membrane i.e. over the beads (Column 6, lines 45-47) and McDevitt et al teach the similar array wherein the hybridization chamber comprises a flexible membrane (Column 11, line s 40-44).

Regarding Claims 82 and 106, Walt et al teach the depressions are wells (Column 6, lines 16-30). McDevitt et al teach the similar array wherein the depressions are wells (Fig. 3) and Seul et al teach the similar array wherein the depressions are wells formed via hydrophobic grid (Column 23, lines 9-15).

Regarding Claim 107-108, Walt et al teach the method further comprising preparation of the DNA by PCR (Column 23, lines 5-8).

Regarding Claim 109-111, Walt et al teach the method wherein the bioactive agent is DNA (Column 10, lines 28-35) and the method includes sequencing (Column 24, lines 51-52). While Walt et al teaches the array is used for sequencing, the sequencing practiced with the array produced by the method, does not further define the method of making the array. As such, the recited sequencing methods do not

further define the method of Claim 94 for making the array. Furthermore, Felder et al teaches the similar method determines the sequence (column 11, lines 23-48).

Regarding Claims 95-96, 112-117, Walt et al teach the arrays and methods wherein each subpopulation is randomly distributed such that members of each subpopulation are in multiple sub-bundles (Column 18, line 48-Column 19, line 53). Seul et al teach the similar array wherein each subpopulation is randomly distributed such that members of each subpopulation are in each assay location (Fig. 28, Column 44, lines 43-67).

Regarding Claims 126, 129, 131 and 132, Seul et al teach the similar array wherein hybridization between the target and bean-immobilized capture probe occur prior to bead immobilization on the support thereby providing both double and single stranded nucleic acids on the beads. Seul teaches that hybridization prior to surface immobilization facilitate subsequent analysis of strands of interest (Column 32, line 62-Column 33, line 7). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the solution hybridization prior to immobilization as taught by Seul to the array and method of Walt. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success and for the added benefit of facilitating subsequent analysis of strands of interest as desired in the art (Seul, Column 32, line 62-Column 33, line 7).

Regarding Claim 134-141,Walt teaches the array and methods providing one bead/depression thereby providing no more than one bead from each of the first and second population (Column 17, lines 3-10).

7. Claims 65, 67, 70, 76, 78, 81, 88, 90, 93, 101, 102, 105, 126, 128, 130, 133 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (U.S. Patent No. 6,327,410, filed 11 September 1998) in view of McDevitt et al (U.S. Patent No. 6,680,206, filed 16 July 1999) and/or Seul et al (U.S. Patent No. 7,041,510, filed 17 September 1999) as applied to Claims 60, 71, 83, 94 above and further in view of Felder et al (U.S. Patent No. 6,232,066, filed 2 July 1998).

Regarding Claims 65, 70, 76, 81, 88, 93, 101, 105, 126, 130, 133, Walt et al teach the assay locations are spatially identifiable manually but the reference does not specifically teach the assay locations are separated. However, array locations separated by gaskets were well known in the art at the time the claimed invention was made as taught by Felder et al (Fig. 4-5).

Felder et al teach a substrate (Column 5, lines 1-13) having a plurality of assay locations (regions), each having a subpopulation of bioactive agents (e.g. genomic DNA, Column 6, lines 52-67) wherein the assay locations are separated by a gasket forming an array of wells-within-wells (e.g. wax or silicone barriers/well separator, Column 5, lines 19-59; Column 6, lines 38-51; Column 13, lines 1-22; and Fig. 5) whereby the assay locations are spatially discrete, identifiable and addressable within a fluidically controlled environment (Column 5, lines 19-59).

Walt clearly desires segregation of the subpopulations to provide spatial encoding of the microspheres and suggests manual techniques to do so (Column 18,

line 59-Column 19, line 5). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the barrier elements of Felder et al to the substrate of Walt et al. One of ordinary skill in the art would have been motivated to do so based on the desired segregation of Walt et al and further for the expected benefit of providing for fluidically controlled multi-sample testing without cross contamination between adjacent regions as taught by Felder et al (Column 5, lines 19-59).

Regarding Claim 67, 78, 90, 102, Walt et al teach the array wherein the support is planar glass (Column 5, lines 57-60). McDevitt (Column 8, line 64) and Seul (Column 9, line 46) also teach glass substrate. Felder et al teach the similar array wherein the glass support is a glass slide (Column 5, line 2). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the slide of Felder to the glass substrates of Walt, McDevitt and/or Seul. One of ordinary skill in the art would have been motivated to do so based on the commercial availability of microscope slides.

NEW GROUNDS FOR REJECTION NECESSITATED BY NEW CLAIMS 142-157

8. Claims 142-146, 149-154 and 157 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (U.S. Patent No. 6,327,410, filed 11 September 1998) as evidenced by Chee (U.S. Patent No. 6,544,732, filed 20 May 1999) in view of McDevitt et al (U.S. Patent No. 6,680,206, filed 16 July 1999) and/or Seul et al (U.S. Patent No.

7,041,510, filed 17 September 1999) and Drmanac et al (EP 0392546, published 17 October 1990).

Regarding Claims 142-146 and 150-154, Walt et al disclose an array and method of making the array comprising a substrate having a surface (Column 5, lines 32-60), a first assay location and second assay location on the surface (Column 5, line 61-Column 6, line 30), wherein the substrate has a first plurality of depressions in first and second assay locations and first and second microsphere populations randomly placed in the assay locations wherein the assay locations spatially identifiable (Column 18, line 59-Column 18, line 5).

Walt teaches the array and method wherein the bioactive agents are attached to "blank microspheres" to provide the subpopulations (Column 12, lines 3-8). Chee (Column 8, lines 23-27) teaches:

> Each microsphere comprises a bioactive agent, although as will be appreciated by those in the art, there may be some microspheres which do not contain a bioactive agent, depending the on the synthetic methods.(emphasis added)

Hence, one of skill in the art would appreciate that each population of Walt would likely include a subpopulation of blank microspheres.

Furthermore, blank beads were well known and routinely practiced in the art of bead arrays at the time the invention was made as taught by McDevitt and Seul.

McDevitt et al teach a similar array and method of making the array comprising a substrate having a surface (Fig. 3), a first assay location and second assay location on the surface (#250, Fig. 3, Column 39, lines 15-34 and Column 40, lines 34-37), a first

plurality of depressions in first and second assay locations and first and second microsphere populations randomly placed in the assay locations (Column 10, lines 13-16) and wherein assay locations comprises blank microspheres (Column 25, lines 1-45 and Fig. 16) wherein the blank microspheres provide a reference signal to which multiple different signals can be compared thereby allowing simultaneous evaluation of multiple chemically distinct analytes (Column 25, lines 1-8).

Seul also teach a similar array and method of making the array comprising a substrate having multiple assay locations and multiple populations of beads randomly distributed in the assay locations (e.g. Fig. 28) wherein the assay locations further comprise blank beads (i.e. spacer particles) to provide interparticle spacing of analyte beads and thereby allowing optical analysis of individual analyte particles (Column 25, lines 2-21).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the blank beads of McDevitt and/or Seul to the array of Walt. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success and for the added benefits of providing appropriate spacing of analyte beads allowing optical analysis of individual analyte particles (Seul, Column 25, lines 2-21) and/or providing a reference signal to which multiple different signals can be compared allowing simultaneous evaluation of multiple chemically distinct analytes (McDevitt, Column 25, lines 1-8).

Walt teaches that the microparticles have an optical signature generated by a mixture of dyes so as to distinguish subpopulations of microspheres based on the

signature (Column 13, lines 8-30) but does not teach an optical signature provided by a combination of oligonucleotides. However, oligo-tagged microspheres were well known in the art at the time the invention was made as taught by Drmanac.

Drmanac teaches an array and method for making an array of randomly distributed discrete particles (DP)(Abstract) wherein the array comprises subpopulations of DNA molecules are attached to the DP which are encoded by combinations of dye-labeled oligotags (Column 7, lines 50-58 and Columns 14-16). Drmanac teaches hybridization of complementary nucleic acids to decode the DP (paragraph spanning Columns 7-8) wherein the nucleic acids are 8-40 in length (Columns 14-16). Drmanac teaches that 20 oligotags can be combined to differentially encoded 10^5 DP (paragraph spanning columns 7-8).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the oligotag encoding of Drmanac to the microspheres of Walt. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success based on the teaching of Drmanac. The artisan would have been further motivated do so to obtain the high order encoding desired in the art (Drmanac, Abstract and paragraph spanning columns 7-8).

Regarding Claims 149 and 157, Walt et al teach the array is within a hybridization chamber (Fig. 4). McDevitt et al teach the similar array wherein the substrate is enclosed within a hybridization chamber (Fig. 17, Column 26-27).

9. Claims 147-148 and 155-156 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (U.S. Patent No. 6,327,410, filed 11 September 1998) in view of McDevitt et al (U.S. Patent No. 6,680,206, filed 16 July 1999) and/or Seul et al (U.S. Patent No. 7,041,510, filed 17 September 1999) and Drmanac et al (EP 0392546, published 17 October 1990) as applied to Claims 142 and 150 above and further in view of Felder et al (U.S. Patent No. 6,232,066, filed 2 July 1998).

Regarding Claims 147 and 155, Walt et al teach the assay locations are spatially identifiable manually but the reference does not specifically teach the assay locations are separated. However, array locations separated by gaskets were well known in the art at the time the claimed invention was made as taught by Felder et al (Fig. 4-5).

Felder et al teach a substrate (Column 5, lines 1-13) having a plurality of assay locations (regions), each having a subpopulation of bioactive agents (e.g. genomic DNA, Column 6, lines 52-67) wherein the assay locations are separated by a gasket forming an array of wells-within-wells (e.g. wax or silicone barriers/well separator, Column 5, lines 19-59; Column 6, lines 38-51; Column 13, lines 1-22; and Fig. 5) whereby the assay locations are spatially discrete, identifiable and addressable within a fluidically controlled environment (Column 5, lines 19-59).

Walt clearly desires segregation of the subpopulations to provide spatial encoding of the microspheres and suggests manual techniques to do so (Column 18, line 59-Column 19, line 5). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the barrier elements of Felder et al to the substrate of Walt et al. One of ordinary skill in the art would have been

motivated to do so based on the desired segregation of Walt et al and further for the expected benefit of providing for fluidically controlled multi-sample testing without cross contamination between adjacent regions as taught by Felder et al (Column 5, lines 19-59).

Regarding Claims 148 and 156, Walt et al teach the array wherein the support is planar glass (Column 5, lines 57-60). McDevitt (Column 8, line 64) and Seul (Column 9, line 46) also teach glass substrate. Felder et al teach the similar array wherein the glass support is a glass slide (Column 5, line 2). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the slide of Felder to the glass substrates of Walt, McDevitt and/or Seul. One of ordinary skill in the art would have been motivated to do so based on the commercial availability of microscope slides.

Response to Arguments

10. Applicant argues that the combination of Walt and McDevitt does not teach or suggest random distribution of blank microspheres at first and second assay locations. Applicant provides a discussion of McDevitt and acknowledges that the reference teaches blank particles and further acknowledges that the reference teaches random placement of particles (Response, page 14, lines 1-7). However, Applicant argues that McDevitt does not teach random distribution of blank particles as claimed. Applicant states that the blank particles or McDevitt are used as negative controls that provide a reference signal for comparison. Applicant asserts that the negative controls are only valuable if the location of the blank is known and therefore the blank particles (i.e.

negative controls) of McDevitt cannot be randomly distributed. Applicant further argues that the ordinary artisan would not be motivated to randomly distribute the blank particles of McDevitt in the array of Walt because the location of negative controls must be known.

The arguments are not found persuasive. Applicant acknowledges that McDevitt teaches random placement of particles and also teaches blank particles (Response, page 14, lines 1-7). Applicant's arguments appear to be based on the fact that McDevitt does not anticipate the invention by teaching random distribution of both analyte and blank particles. However, the rejection is based on the combined teaching of Walt and McDevitt.

Walt teaches the array and method wherein the bioactive agents are attached to "blank microspheres" to provide the subpopulations (Column 12, lines 3-8). Chee (Column 8, lines 23-27) teaches:

> Each microsphere comprises a bioactive agent, although as will be appreciated by those in the art, there may be some microspheres which do not contain a bioactive agent, depending the on the synthetic methods.(emphasis added)

Hence, one of skill in the art would appreciate that each population of Walt would likely include a subpopulation of blank microspheres.

Additionally, Walt specifically teaches an array comprising multiple subpopulations of microspheres and random distribution of each subpopulation of microspheres via e.g. serial loading of the array (Column 17, lines 46-55, Column 19, lines 31-53). Walt teaches sequential addition of subpopulations to the array. After the

addition of each subpopulation, the array is decoded to determine the location of each microsphere of the subpopulation. The addition and decoding is repeated for each subpopulation (Column 19, lines 31-53). Thus, Walt randomly distributes each subpopulation and then decodes the array so that the position of each microsphere is known prior to using and/or reading the array in the presence of analyte.

In a similar fashion, McDevitt randomly distributes the particles and then determines the positions of the particles prior to use (Column 10, lines 13-17). While this passage of McDevitt does not mention the blank particles, the passage describes the method of making the array and the reference teaches the arrays have blank particles. The passage does not define the random distribution applies only to analyte particles as asserted by Applicant. Given that McDevitt defines the array as having blank particles and further defines the method of making the array by random distribution of particles, it is reasonable to assume that the random distribution includes blank particles. Applicant's arguments regarding known positions for the blank particles is not relevant to the claims. However, it is noted that both Walt and McDevitt teach random distribution of particles followed by determining the positions of the particles prior to use. Furthermore, as discussed above, McDevitt provides the motivation for using blank particles and thus reasons for providing the array of Walt with blank particles.

For all the reasons above, it is maintained that the combination of Walt and McDevitt obviates the invention as claimed.

Applicant argues that the combination of Walt and Seul does not teach the invention and specifically that Seul does not teach random distribution of blank particles. Applicant acknowledges that Seul uses inert spacer beads to adjust interparticle distance but asserts that the reference does not teach blank particles as claimed. Applicant further argues that the particles of Seul are random with respect to chemical identity by are spatially ordered. Applicant states that since “blank microspheres do not have a chemical identity, they cannot be randomly distributed with respect to chemical identity, which is the only type of random distribution disclosed by Seul". Applicant further argues that one of ordinary skill would not be motivated to combine the spacer beads of Seul with the array of Walt because Walt does not teach a contiguous array of bead clusters.

The arguments are not found convincing. First, Walt teaches random deposition of subpopulations. Thus, the claim requirement of random deposition is met my the teaching of Walt. As Applicant notes, Seul illustrates a random array of particles at Fig. 28. Seul (Column 44, lines 49-67) provides the following discussion regarding Fig. 28:

> FIG. 28 illustrates an example with a 4.times.4 matrix having six fields populated with a random array of beads to produce a unique, miniaturized, non-copyable code. Referring now to FIG. 28, therein is illustrated a pattern composed of multiple random encoded arrays of beads produced by the methods disclosed herein. The pattern represents a unique, miniaturized "label" for the substrate on which it is deposited. To design a unique label, positions within an N.times.N matrix to be occupied by bead arrays are randomly chosen. In addition, the

> position of beads within each array is completely random. That is, the structure has two levels of randomness, representing a random matrix of random matrices whose coding capacity is evaluated in the literature. Replication of the label would require the exact, bead-by -bead assembly in accordance with the original structure, a capability that is not required in the original construction where only the top level, that is, the placement of entire arrays of beads into designated position, requires spatial control.

Thus, the random array of Seul is not limited to chemical identity as asserted. In contrast to the assertion, the reference specifically teaches a random array of particles. With regard to the instantly claimed "blank" microspheres, Applicant asserts that the spacer particles of Seul cannot be "blank" because blank microsphere have no chemical identity. The comment is not relevant to the instantly claimed invention. Neither the instant claims nor the specification define blank microspheres as without chemical identity. The specification does provide a non-limiting teaching of blank microspheres (¶ 153 of the pre-grant publication).

> Accordingly, "blank" microspheres may be used that have surface chemistries that facilitate the attachment of the desired functionality by the user. Some examples of these surface chemistries for blank microspheres include, but are not limited to, amino groups including aliphatic and aromatic amines, carboxylic acids, aldehydes, amides, chloromethyl groups, hydrazide, hydroxyl groups, sulfonates and sulfates.

Given the broad definition of "blank microspheres" provided by the instant specification, the inert spacer particles are reasonably encompassed by the instantly claimed blank microspheres.

On page 21 of the Responses, Applicant asserts that the Walt, McDevitt and Seul do not teach depressions within assay locations including microspheres from both first and second subpopulations.

It is maintained that the instantly claimed invention is an obvious variation of Walt. As discussed above, Walt teaches first assay location and second assay location on the surface (Column 5, line 61-Column 6, line 30), wherein the substrate has a first plurality of depressions in first and second assay locations and first and second microsphere populations randomly placed in the assay locations wherein the assay locations spatially identifiable (Column 18, line 59-Column 18, line 5). Walt teaches all the elements of the instantly claimed invention except for the expressed teaching of random distribution of blank microspheres. However, Chee clearly suggests that the subpopulations of Walt would include a subpopulation (i.e. second subpopulation) of blank microspheres. Walt's random distribution would randomly distribute the first subpopulation including the second subpopulations. Thus, given the evidence of Chee, the array and method of Walt include the blank microspheres. Furthermore, as discussed extensively above McDevitt and Seul teach blank microspheres and reasons for adding them to the array of Walt. It is maintained that the prior art teaches all the elements of the instantly claimed invention.

Conclusion

11. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BJ Forman
Primary Examiner
Art Unit 1634

/BJ Forman/
Primary Examiner, Art Unit 1634